JUN 2 4 2004 3

FORM PTO-1449/A and B (Malified)

INFORMATION DISCLUSURE STATEMENT BY APPLICANT

APPLICATION NO.: 10/821,809

ATTY. DOCKET NO.: P0453.70116US01

FILING DATE:

April 8, 2004

CONFIRMATION NO.: Not Yet Assigned

APPLICANT:

Sanghvi et al.

Sheet 1 of 6

GROUP ART UNIT: 2 2 /2 /

EXAMINER:

SPIVACK

U.S. PATENT DOCUMENTS

Examiner's	Cite	U.S. Patent Doo	cument	Name of Patentee or Applicant of Cited	Date of Publication or of issue	
Initials	No.	Number	Kind Code	Document	of Cited Document MM-DD-YYYY	
99	A1	2001/0018413	Al	Crain, et al.	08-30-2001	
Ti	A2	2002/0028825	A1	Foss, et al.	03-07-2002	
	А3	2001/0033865	A1	Oshlack, et al.	10-25-2001	
	A4	2001/0036476	A1	Oshlack, et al.	11-01-2001	
	A5	2001/0047005	A1	Farrar, et al.	11-29-2001	
	A6	4,176,186		Goldberg, et al.	11-27-1979	
	A7	4,719,215		Goldberg	01-12-1988	
	A8	4,861,781		Goldberg	08-29-1989	
	A9	4,987,136		Kreek, et al.	01-22-1991	
	A10	5,102,887		Goldberg	04-07-1992	
	A11	5,270,328		Cantrell, et al.	12-14-1993	
	A12	5,472,943		Crain, et al.	12-05-1995	
	A13	5,512,578		Crain, et al.	04-30-1996	
	A14	5,767,125		Crain, et al.	06-16-1998	
	A15	5,811,451		Minoia, et al.	09-22-1998	
	A16	5,866,164		Kuczynski, et al.	02-02-1999	
	A17	5,958,452		Oshlack, et al.	09-28-1999	
	A18	5,972,954		Foss, et al.	10-26-1999	
	A19	6,096,756		Crain, et al.	08-01-2000	
	A20	6,194,382	B 1	Crain, et al.	02-27-2001	
	A21	6,261,599	B1	Oshlack, et al.	07-17-2001	
•	A22	6,274,591	B1	Foss, et al.	08-14-2001	
	A23	6,395,705	B2	Crain, et al.	05-28-2002	
	A24	6,419,959	B1	Walter, et al.	07-16-2002	
	A25	6,451,806	B2	Farrar	09-17-2002	
	A26	6,559,158	B1	Foss, et al.	05-06-2003	
	A27	6,608,075	B1	Foss, et al.	08-19-2003	
	A28	RE36,547		Crain, et al.	02-01-2000	
V	A29	2002/0188005	A1	Farrar, et al.	12-12-2002	

FOREIGN PATENT DOCUMENTS

Examiner's	Cite	Foreign Patent Document			Name of Patentee or Applicant of Cited	Date of Publication of	Translation
Initials	No.	Office/ Country	Number	Kind Code	Document (not necessary)	Cited Document MM-DD-YYYY	(Y/N)
1/5	B1	AU	610,561		Shelley	08-17-1988	
7/5	B2	CA	1,315,689		The University of Chicago	04-06-1993	
$\Box IS$	В3	EP	0278821	Al	Shelly (Abstract)	08-17-1988	

800408.1

Phyllis Spivack sp

5/2/07

APPLICATION NO.: 10/821,809 FORM PTO-1449/A and B (Modified) ATTY. DOCKET NO.: P0453.70116US01 INFORMATION DISCLOSURE **FILING DATE:** April 8, 2004 CONFIRMATION NO.: Not Yet Assigned STATEMENT BY APPLICANT APPLICANT: Sanghvi et al. GROUP ART UNIT: Not Yet Assigned **EXAMINER:** Not Yet Assigned Sheet 2 of 6

85	B4	EP	0352361	A1	The Rockefeller University	01-31-1990	
105	B5	EP	278,821	A1	Marc Yves Shelly (Derwent Abstract) 08-17-1988		
105	B6	EP	306,575	B1	The Univ. of Chicago	03-15-1989	
105	B7	EP	352,361	Al	The Rockefeller University	01-31-1990	
100	B8	EP	760,661	B1	Minoia, et al.	12-30-1998	
R	B9	JР	2,625,457	B2	Goldberg (Derwent Abstract)	07-02-1997	
1	B10	NZ	222,911		The Univ. of Chicago	12-14-1987	
051	B11	wo	83/03197	A1	The Rockefeller University	09-29-1983	
1	B12	wo	88/05297	A1	Shelly	07-28-1988	
1/1	B13	wo	95/31985	A2	Minoia, et al.	11-30-1995	
1K	B14	wo	97/33566		Alza Corp.	09-18-1997	
105	B15	wo	98/25613		Klinge Pharma GmbH	06-18-1998	Yes
TIC	B16	wo	01/13909	A2	Critical Care Pharm.	03-01-2001	
15	B17	wo	01/37785	A2	Adolor Corp.	05-31-2001	
11/5	B18	wo	01/41705	A2	Adolor Corp.	06-14-2001	
105	B19	wo	01/42207	A2	Adolor Corp.	06-14-2001	
12 12	B20	wo	01/85257	A2	Pain Therapeutics, Inc	11-15-2001	
T DS	B21	wo	02/060870	A2	Adolor Corp.	08-08-2002	

Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item Translation Examiner's Cite (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), (Y/N) Initials No publisher, city and/or country where published. AKINBAMI et al., Effect of a peripheral and a central acting opioid antagonist on the testicular response to C1 stress in rats. Neuroendocrinology. 1994 Apr;59(4):343-8. AMIN et al., Efficacy of methylnaltrexone versus naloxone for reversal of morphine-induced depression of C2 hypoxic ventilatory response. Anesth Analg. 1994 Apr;78(4):701-5. AMIR, Naloxone improves, and morphine exacerbates, experimental shock induced by release of endogenous histamine by compound 48/80. Brain Res. 1984 Apr 9;297(1):187-90. C3 AMIR et al., Endorphins in endotoxin-induced hyperglycemia in mice. Arch Toxicol Suppl. 1983;6:261-5. C4 ARGENTIERI et al., Interaction of the opiate antagonist, naltrexone methyl bromide, with the acetylcholine C5 receptor system of the motor end-plate. Brain Res. 1983 Oct 31;277(2):377-9. BARATTI et al., Brain opioid peptides may participate in the reversal of pentylenetetrazol-induced amnesia. C6 Methods Find Exp Clin Pharmacol. 1990 Sep;12(7):451-6. BEDINGFIELD et al., Methylnaltrexone attenuates taste aversion conditioned by low-dose ethanol. Alcohol. **C7** 1998 Jan; 15(1):51-4. BIANCHETTI et al., Quaternary derivatives of narcotic antagonists; stereochemical requirements at the chiral C8 nitrogen for in vitro and in vivo activity. Life Sci. 1983;33 Suppl 1:415-8. BIANCHI et al., Quaternary narcotic antagonists' relative ability to prevent antinociception and gastrointestinal transit inhibition in morphine-treated rats as an index of peripheral selectivity. Life Sci. 1982 May C9 31;30(22):1875-83. BICKEL, Stimulation of colonic motility in dogs and rats by an enkephalin analogue pentapeptide. Life Sci. C10 1983;33 Suppl 1:469-72. BLANK et al., Central, stereoselective receptors mediate the acute effects of opiate antagonists on luteinizing C11 hormone secretion. Life Sci. 1986 Oct 27;39(17):1493-99. BRIX-CHRISTENSEN et al., Endogenous morphine is produced in response to cardiopulmonary bypass in C12 neonatal pigs. Acta Anaesthesiol Scand. 2000 Nov;44(10):1204-8. BROWN et al., Opiate antagonists: central sites of action in suppressing water intake of the rat. Brain Res., 1981,

OTHER ART — NON PATENT LITERATURE DOCUMENTS

Phyllis Spiwack

Sep 28;221(2):432-6.

C13

5/27/07

FORM PTO-1449/A and B (Modified)				APPLICATION NO.:	10/821,809	ATTY. DOCKET NO.: P0453.70116US01
Ī	RMATION D			FILING DATE:	April 8, 2004	CONFIRMATION NO.: Not Yet Assigned
STAT	EMENT BY	APP	PLICANT	APPLICANT:	APPLICANT: Sanghvi et al.	
				GROUP ART UNIT:	Not Vet Assigned	EXAMINER: Not Yet Assigned
Sheet	3	of	6	OKOO! AK! ON!!.		DAMMILLA. NOT TO ASSIGNED

ns	C14	BROWN et al., Reversal of morphine-induced catalepsy in the rat by narcotic antagonists and their quaternary derivatives. Neuropharmacology. 1983 Mar;22(3):317-21.									
DS.		BROWN et al., The use of quaternary narcotic antagonists in opiate research. Neuropharmacology. 1985									
1/2	C15	Mar;24(3):181-91. Review.									
bs	CALCAGNETTI et al., Quaternary naltrexone reveals the central mediation of conditional opioid analgesia. Pharmacol Biochem Behav. 1987 Jul;27(3):529-31.										
H-7-		CHANG et al., An antiabsorptive basis for precipitated withdrawal diarrhea in morphine-dependent rats. J									
15	C17	Pharmacol Exp Ther. 1984 Feb;228(2):364-9.									
\ \alpha \		CULPEPPER-MORGAN et al., Treatment of opioid-induced constipation with oral naloxone: a pilot study. Clin									
11/5	C18	Pharmacol Ther. 1992 Jul;52(1):90-5 (ABSTRACT ONLY). EISENBERG, Effects of naltrexone on plasma corticosterone in opiate-naive rats: a central action. Life Sci.									
105	C19	1984 Mar 19;34(12):1185-91.									
125	C20	FERNANDEZ-TOME et al., Interaction between opioid agonists or naloxone and 5-HTP on feeding behavior in food-deprived rats. Pharmacol Biochem Behav. 1988 Feb;29(2):387-92.									
 	020	1000-depired lats. I hamilated Blockient Bellay, 1900 1 et 22/2/30192.									
1/25,	C21	FOSS, A review of the potential role of methylnaltrexone in opioid bowel dysfunction. Am J Surg. 2001 Nov;182(5A Suppl):19S-26S. Review.									
1		FOSS et al., 1995 Annual scientific meeting of the American Society of Anesthesiologists. Atlanta, Georgia,	- 1								
	C22	October 21-25, 1995. Abstracts. Anesthesiology. 1995 Sep;83(3A Suppl):A361.									
100		FOSS et al., Prevention of apomorphine- or cisplatin-induced emesis in the dog by a combination of									
	C23	methylnaltrexone and morphine. Cancer Chemother Pharmacol. 1998;42(4):287-91.									
n		FOSS et al., Safety and tolerance of methylnaltrexone in healthy humans: a randomized, placebo-controlled,	ļ								
1/5 \	C24	intravenous, ascending-dose, pharmacokinetic study. J Clin Pharmacol. 1997 Jan;37(1):25-30.									
1001		FOSS et al., Dose-related antagonism of the emetic effect of morphine by methylnaltrexone in dogs. J Clin									
199	C25	Pharmacol. 1993 Aug;33(8):747-51.									
		FOSS et al., Effects of methylnaltrexone on morphine-induced cough suppression in guinea pigs. Life Sci.									
1 125	C26	1996;59(15):PL235-8.									
 	020	FOSS et al., Methylnaltrexone reduces morphine-induced postoperative emesis by 30%. Anesth Analg.									
1921	C27	1994;78:S119.	İ								
177	021	FRANCE et al., Comparison of naltrexone and quaternary naltrexone after systemic and intracerebroventricular									
l ns	000										
11/2	C28	administration in pigeons. Neuropharmacology. 1987 Jun;26(6):541-8.									
1 DS		FRANCE et al., Intracerebroventricular drug administration in pigeons. Pharmacol Biochem Behav. 1985	}								
182	C29	Nov;23(5):731-6.									
1 100		FRIEDMAN et al., Opioid antagonists in the treatment of opioid-induced constipation and pruritus. Ann	Ì								
. [7]	C30	Pharmacother. 2001 Jan;35(1):85-91. Review.									
na \		GMEREK et al., Independent central and peripheral mediation of morphine-induced inhibition of									
VK	C31	gastrointestinal transit in rats. J Pharmacol Exp Ther. 1986 Jan;236(1):8-13.									
		HEIN et al., Pharmacological analysis of the discriminative stimulus characteristics of ethylketazocine in the									
(/<	C32	rhesus monkey. J Pharmacol Exp Ther. 1981 Jul;218(1):7-15.									
N	C33	HOWD et al., Naloxone and intestinal motility. Experientia. 1978 Oct 15;34(10):1310-1.									
 \\ \ \ \ 		JALOWIEC et al., Suppression of juvenile social behavior requires antagonism of central opioid systems.									
1 1 ns	C34	Pharmacol Biochem Behav. 1989 Jul;33(3):697-700.									
	007	JANKOVIC et al., Quaternary naltrexone: its immunomodulatory activity and interaction with brain delta and									
181	C35	kappa opioid receptors. Immunopharmacology. 1994 Sep-Oct;28(2):105-12.									
		KAUFMAN et al., Role of opiate receptors in the regulation of colonic transit. Gastroenterology. 1988									
1 125	C36	Jun;94(6):1351-6.									
	<u> </u>	KIM et al., Assay for methylnaltrexone in rat brain regions and serum by high-performance liquid									
1251	C37	chromatography with coulometric electrochemical detection. Chromatographia. 1989 Oct;28(7-8):359-63.	1								
1 h	 	KINSMAN et al., Effect of naloxone on feedback regulation of small bowel transit by fat. Gastroenterology.									
1 PS	C38	1984 Aug;87(2):335-7.	ŀ								
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		KOBLISH et al., Behavioral profile of ADL 8-2698, a novel GI-restricted μ opioid receptor antagonist. Society									
1 X	C39	for Neuroscience Abstracts. 2001;27(2):2407.									
1 1 x x	1000	KOBYLECKI et al., N-Methylnalorphine: definition of N-allyl conformation for antagonism at the opiate									
1 125	C40	receptor. J Med Chem. 1982 Nov;25(11):1278-80.									
1 Oct	C41	KOCZKA, et al., Acta Chimica Academica Scien. Hung. (1967) 51(4), 393-02									
	1 041	g. (·								

Phyllis Spivack shifter

FORM PTC)-1449//	A and B (M	1odifie	d)		APPLICATION NO.:	10/821,809	ATTY. DOCKET NO.: P0453.70116US01
				LOSURI		FILING DATE:	April 8, 2004	CONFIRMATION NO.: Not Yet Assigned
STATEMENT BY APPLICANT					Γ	APPLICANT:	Sanghvi et al.	
						GROUP ART UNIT:	Not Vet Assigned	EXAMINER: Not Yet Assigned
Sheet	4		of	6		OROGI 74CI GIVII:		

			Triangle III						
D5	5	C42	KOOB et al., Effects of opiate antagonists and their quaternary derivatives on heroin self-administration in the rat. J Pharmacol Exp Ther. 1984 May;229(2):481-6.						
1	14	KOTAKE et al., Variations in demethylation of N-methylnaltrexone in mice, rats, dogs, and humans. C43 Xenobiotica. 1989 Nov;19(11):1247-54.							
1	1	C44	KROMER et al., Endogenous opioids, the enteric nervous system and gut motility. Dig Dis. 1990;8(6):361-73. Review.						
115	4		KROMER et al., The current status of opioid research on gastrointestinal motility. Life Sci. 1989;44(9):579-89.						
1/2	1	C45 C46	Review. LEANDER, A kappa opioid effect: increased urination in the rat. J Pharmacol Exp Ther. 1983 Jan;224(1):89-94.						
1	V) 	C47	LITTLE, et al., Society for Neuroscience Abstracts, 27 (2); 2001, p. 2407						
→	DC	C48	LIVINGSTON et al., Postoperative ileus. Dig Dis Sci. 1990 Jan;35(1):121-32. Review.	-					
10	 	C49	LYDON et al., ESA Free Paper Prize Competition. Eur J Anaesthesiol. 2001 Apr; 18 Suppl 21:92.						
19	1	<u> </u>	LYSLE et al., Modulation of immune status by a conditioned aversive stimulus: evidence for the involvement of						
1 (1 5	C50	endogenous opioids. Brain Behav Immun. 1992 Jun;6(2):179-88.						
- ' 1	/=		MAGNAN et al., The binding spectrum of narcotic analgesic drugs with different agonist and antagonist						
	MC 1	C51	properties. Naunyn Schmiedebergs Arch Pharmacol. 1982 Jun;319(3):197-205.						
()S	1	C52	MANARA, et al., Adv. Endog. Exog. Opioids, Poroc. Int. Narc. Res. Conf., 12th (1981), 402-4						
1/3	7		MANARA et al., The central and peripheral influences of opioids on gastrointestinal propulsion. Annu Rev						
11	クー	C53	Pharmacol Toxicol. 1985;25:249-73. Review.						
~			MICKLEY et al., Quaternary naltrexone reverses morphine-induced behaviors. Physiol Behav. 1985						
1/2	<u> </u>	C54	Aug;35(2):249-53.						
10	_	0	MISRA et al., Intravenous kinetics and metabolism of [15,16-3H]naltrexonium methiodide in the rat. J Pharm						
14	2	C55	Pharmacol. 1987 Mar;39(3):225-7.						
1 1	OS	C56	MOERMAN et al., Evaluation of methylnaltrexone for the reduction of postoperative vomiting and nausea						
	 	C57	incidences. Acta Anaesthesiol Belg. 1995;46(3-4):127-32. MOSS, et al., N. Engl. J. Med., (2002) 346 (6), 455						
42	1	C57	MUCHA, Is the motivational effect of opiate withdrawal reflected by common somatic indices of precipitated						
ΙΙ.	AC	C58	withdrawal? A place conditioning study in the rat. Brain Res. 1987 Aug 25;418(2):214-20.						
1	///	000	MUCHA, Taste aversion involving central opioid antagonism is potentiated in morphine-dependent rats. Life						
DC]	C59	Sci. 1989;45(8):671-8.						
17	7	C60	MURPHY et al., Anesthesiology, Sept. (1999), 91 (3A) p. A349 (Abstract)						
-19	500		MURPHY et al., Pharmacokinetic profile of epidurally administered methylnaltrexone, a novel peripheral opioid						
. '	いひら	C61	antagonist in a rabbit model. Br J Anaesth. 2001 Jan;86(1):120-2.						
A) C	7		MURPHY et al., American Society of Anesthesiologists 1999 annual meeting. Dallas, Texas, USA. October 9-						
		C62	13, 1999. Abstracts. Anesthesiology. 1999 Sep;91(3A Suppl):A349.						
16	ار ا	000	MURPHY et al., Opioid-induced delay in gastric emptying: a peripheral mechanism in humans. Anesthesiology.						
\vdash	12	C63	1997 Oct;87(4):765-70.						
	15	C64	MURPHY et al., Opioid antagonist modulation of ischaemia-induced ventricular arrhythmias: a peripheral mechanism. J Cardiovasc Pharmacol. 1999 Jan;33(1):122-5.						
- <u>-</u>	4/		NARANJO et al., Evidence for a central but not adrenal, opioid mediation in hypertension induced by brief						
199	ا ۱	C65	isolation in the rat. Life Sci. 1986 May 26;38(21):1923-30.						
1	05	C66	NELSON, Dissertation Abstracts International, (62/03-B), p. 1635 (Abstract)						
m			ODIO et al., Central but not peripheral opiate receptor blockade prolonged pituitary-adrenal responses to stress.						
	1	C67	Pharmacol Biochem Behav. 1990 Apr;35(4):963-9.						
10	$\overline{}$		OSINSKI et al., Determination of methylnaltrexone in clinical samples by solid-phase extraction and high-						
111	9		performance liquid chromatography for a pharmacokinetics study. J Chromatogr B Analyt Technol Biomed Life						
		C68	Sci. 2002 Nov 25;780(2):251-9.						
'	15	C69	PAPPAGALLO, Incidence, prevalence, and management of opioid bowel dysfunction. Am J Surg. 2001						
<u> </u>	5	- CO3	Nov;182(5A Suppl):11S-18S. Review. POLAK et al., Enkephalin-like immunoreactivity in the human gastrointestinal tract. Lancet. 1977 May						
	125	C70	7;1(8019):972-4.						
C			POWELL et al., Paradoxical effects of the opioid antagonist naltrexone on morphine analgesia, tolerance, and						
75	>1	C71	reward in rats. J Pharmacol Exp Ther. 2002 Feb;300(2):588-96.						
	05	C72	QUOCK, et al, J. Bioelectr. (1986), 5(1), 35-46						

800408.

P. Spivack 5/27/07

FORM PTC)-1449/A and B (M	lodifie	d)	APPLICATION NO.:	10/821,809	ATTY. DOCKET NO.: P0453.70116US01	
	RMATION D			FILING DATE:	April 8, 2004	CONFIRMATION NO.: Not Yet Assigned	
STAT	EMENT BY	APP	LICANT	APPLICANT:	Sanghvi et al.		
				GROUP ART UNIT:	Not Vet Assigned	EXAMINER: Not Yet Assigned	
Sheet	5	of	6	GROOT ART CHIT.		Exercising to the second secon	

. '>	C73	QUOCK et al., Narcotic antagonist-induced hypotension in the spontaneously hypertensive rat. Life Sci. 1985 Sep 2;37(9):819-26.	
175	C74	QUOCK et al., Narcotic antagonist potentiation of apomorphine drug effect: a stereospecific, centrally mediated drug action. Prog Neuropsychopharmacol Biol Psychiatry. 1985;9(3):239-43.	
75	C75	RAMABADRAN, Effects of N-methylnaloxone and N-methylnaltrexone on nociception and precipitated abstinence in mice. Life Sci. 1982 Sep 20-27;31(12-13):1253-6.	
105	C76	RIVIÈRE et al., Fedotozine reverses ileus induced by surgery or peritonitis: action at peripheral kappa-opioid receptors. Gastroenterology. 1993 Mar;104(3):724-31.	
05	C77	ROBINSON et al., Oral naloxone in opioid-associated constipation. Lancet. 1991 Aug 31;338(8766):581-2.	
1/5 1	C78	ROGER et al., Colonic motor responses in the pony: relevance of colonic stimulation by opiate antagonists. Am J Vet Res. 1985 Jan;46(1):31-5.	
PS	C79	RUSSELL et al., Antagonism of gut, but not central effects of morphine with quaternary narcotic antagonists. Eur J Pharmacol. 1982 Mar 12;78(3):255-61.	
75	C80	SCHAEFER et al., Effects of opioid antagonists and their quaternary derivatives on locomotor activity and fixed ratio responding for brain self-stimulation in rats. Pharmacol Biochem Behav. 1985 Nov;23(5):797-802.	
1/2	C81	SCHANG et al., Beneficial effects of naloxone in a patient with intestinal pseudoobstruction. Am J Gastroenterol. 1985 Jun;80(6):407-11.	
15	C82	SCHANG et al., How does morphine work on colonic motility? An electromyographic study in the human left and sigmoid colon. Life Sci. 1986 Feb 24;38(8):671-6.	
12:	C83	SCHILLER et al., Studies of the mechanism of the antidiarrheal effect of codeine. J Clin Invest. 1982	
100	C84	Nov;70(5):999-1008. SCHMIDHAMMER, et al., Helv. Chim. Acta (1994), Vol. 77, No. 6, p. 1585-9	
 	C85	SCHMIDHAMMER, et al., Helv. Chim. Acta (1994), Vol. 17, No. 0, p. 1383-97 SCHMIDHAMMER, et al., Helv. Chim. Acta (1993) No. 1, p. 476-80.	
1 / K	C86	SCHOLZ, 2000, 63 (6) p. 103,	
1-1/2	C00	SCHOLE, 2000, 63 (6) p. 103. SCHREIER et al., Central regulation of intestinal function: morphine withdrawal diarrhea. Proc West Pharmacol	
1 <i>VS</i> 1 1	C87	Soc. 1982;25:151-4.	
10-		SOLVASON et al., Naltrexone blocks the expression of the conditioned elevation of natural killer cell activity in	
L'_1/5	C88	BALB/c mice. Brain Behav Immun. 1989 Sep;3(3):247-62.	
	C89	SWAN, et al., AIDS Research, NIDA Notes, (1995), 10(3), 1-6	
1.7/5	C90	SYKES, Oral naloxone in opioid-associated constipation. Lancet. 1991 Jun 15;337(8755):1475.	
25	C91	TAGUCHI et al., Selective postoperative inhibition of gastrointestinal opioid receptors. N Engl J Med. 2001 Sep 27;345(13):935-40.	
1.05	C92	THOMPSON et al., Opioid stimulation in the ventral tegmental area facilitates the onset of maternal behavior in rats. Brain Res. 1996 Dec 16;743(1-2):184-201.	
BS	C93	UKAI et al., Suppression of deprivation-induced water intake in the rat by opioid antagonists: central sites of action. Psychopharmacology (Berl). 1987;91(3):279-84.	
PS	C94	VALENTINO et al., Quaternary naltrexone: evidence for the central mediation of discriminative stimulus effects of narcotic agonists and antagonists. J Pharmacol Exp Ther. 1981 Jun;217(3):652-9.	
2	C95	VALENTINO et al., Receptor binding, antagonist, and withdrawal precipitating properties of opiate antagonists. Life Sci. 1983 Jun 20;32(25):2887-96.	
125	C96	WALKER, et al., Psychopharmacology (1991), 104(2), p. 164-6	
PSn	-	WARREN et al., Effects of quaternary naltrexone and chlordiazepoxide in squirrel monkeys with enhanced	
	C97	sensitivity to the behavioral effects of naltrexone. J Pharmacol Exp Ther. 1985 Nov;235(2):412-7.	
12/2	C98	WILLETTE, et al., Res. Commun. Subst. Abuse (1983), 4(4), 325-37.	
	C99	YUAN et al., Drug Dev. Res. (2000) 50(2), 133-141,	
12	C100	YUAN et al., Gastric effects of methylnaltrexone on mu, kappa, and delta opioid agonists induced brainstem unitary responses. Neuropharmacology. 1999 Mar;38(3):425-32.	
112	C100	YUAN et al., Anesthesiology, Sept. (1995), 83 (3A), p A358 (Abstract)	
1 12	C102	YUAN et al., Anesthesiology, Sept. (1995), 83 (3A), p A360 (Abstract)	
DS 19	C103	YUAN et al., Anesthesiology, Sept. (1999), 91 (3A) p. A973 (Abstract)	
	3.00	YUAN et al., Effects of enteric-coated methylnaltrexone in preventing opioid-induced delay in oral-cecal transit	
1 1/5	C104	time. Clin Pharmacol Ther. 2000 Apr;67(4):398-404.	<u> </u>
1tx	C105	YUAN et al., The safety and efficacy of oral methylnaltrexone in preventing morphine-induced delay in oral-	
40	C105	cecal transit time. Clin Pharmacol Ther. 1997 Apr;61(4):467-75.	

800408.1

Phyllis Spiract

5/27/07

FORM PTO)-1449/A and B (M	lodifie	d)	APPLICATION NO.:	10/821,809	ATTY. DOCKET NO.: P0453.70116US01	
1	RMATION D			FILING DATE:	FILING DATE: April 8, 2004 CONFIRMATION NO.		
. STAT	EMENT BY	APP	LICANT	APPLICANT:	APPLICANT: Sanghvi et al.		
				GROUP ART UNIT:	Not Vet Assigned	EXAMINER: Not Yet Assigned	
Sheet	6	of	6	GROOF ART OWN.	110t Tet Assigned	EXAMINER. Not 1 of Assigned	

.79	2	C106	YUAN et al., Methylnaltrexone prevents morphine-induced delay in oral-cecal transit time without affecting analgesia: a double-blind randomized placebo-controlled trial. Clin Pharmacol Ther. 1996 Apr;59(4):469-75.	
19/	ク	.C107	YUAN, et al., Clinical Pharmacology & Therapeutics (1995) 57(2), p. 138	
1	<u>}</u>	C108	YUAN et al., Efficacy of orally administered methylnaltrexone in decreasing subjective effects after intravenous morphine. Drug Alcohol Depend. 1998 Oct 1;52(2):161-5.	
PS		C109	YUAN et al., Effects of methylnaltrexone on morphine-induced inhibition of contraction in isolated guinea-pig ileum and human intestine. Eur J Pharmacol. 1995 Mar 24;276(1-2):107-11.	
TR	5.	C110	YUAN et al., Effects of subcutaneous methylnaltrexone on morphine-induced peripherally mediated side effects: a double-blind randomized placebo-controlled trial. J Pharmacol Exp Ther. 2002 Jan;300(1):118-23.	
14	15	C111	YUAN et al., Oral methylnaltrexone for opioid-induced constipation. JAMA. 2000 Sep 20;284(11):1383-4.	
1/5		C112	YUAN et al., Methylnaltrexone for reversal of constipation due to chronic methadone use: a randomized controlled trial. JAMA. 2000 Jan 19;283(3):367-72.	
P	5	C113	YUAN et al., Effects of intravenous methylnaltrexone on opioid-induced gut motility and transit time changes in subjects receiving chronic methadone therapy: a pilot study. Pain. 1999 Dec;83(3):631-5.	
17	PS	C114	YUAN et al., Effects of methylnaltrexone on chronic opioid induced gut motility and transit time changes. Br J Anaesth. 1998;81(1):94.	
75		C115	YUAN et al., Effects of methylnaltrexone on chronic opioid-induced gut motility and transit time changes. University of Leicester – Abstracts from the Eighth International Symposium on Pain, Anaesthesia and Endocrinology. 1997 September 18-19th.	
775	7	C116	Oncology. 1996;10(12):1880.	

EXAMINER	Phullis Sawack	DATE CONSIDERED SIZIOZ

#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. ___, filed ___, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

[NOTE - Must provide a copy of any patent, publication, other information listed, even if it was previously submitted to, or cited by, the U.S. Patent Office in an earlier application, unless the earlier application is identified by the IDS and is relied upon for an earlier filing date under 35 U.S.C. §120, and the copy was provided in the earlier application.]

APPLICATION NO.: 10/821,809 ATTY. DOCKET NO.: P0453.70116US01

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

APPLICANT: Sanghvi et al.

GROUP ART UNIT: 1614

EXAMINER:

U.S. PATENT DOCUMENTS

Examiner's	Cite	U.S. Patent Docu	ment	Name of Patentee or Applicant of Cited	Date of Publication or of issue	
Initials No.		Number	Kind Code	Document	of Cited Document MM-DD-YYYY	
15	A30	4,311,833		Namikoshi, et al.	01-19-1982	
Tí	A31	4,377,568		Chopra, et al.	03-22-1983	
	A32	4,385,078		Onda, et al.	05-24-1983	
	A33	4,457,907		Porter, et al.	07-03-1984	
	A34	4,462,839		McGinley, et al.	07-31-1984	
	A35	4,518,433		McGinley, et al.	05-21-1985	
	A36	4,556,552		Porter, et al.	12-03-1985	
	A37	4,606,909		Bechgaard, et al.	08-19-1986	
	A38	4,615,885		Nakagame, et al.	10-07-1986	
	A39	4,670,287		Tsuji, et al.	06-02-1987	
	A40	4,857,833		Sherman, et al.	08-15-1999	
	A41	4,888,346		Bihari, et al.	12-19-1989	
	A42	5,426,112		Zagon, et al.	06-20-1995	
	A43	5,536,507		Abramowitz, et al.	07-16-1996	
	A44	5,567,423		Ying, et al.	10-22-1996	
	A45	5,591,433		Michael, et al.	01-07-1997	
	A46	5,597,564		Ying, et al.	01-28-1997	
	A47	5,609,871		Michael, et al.	03-11-1997	
	A48	5,614,222		Kaplan, et al.	03-25-1997	
	A49	5,626,875		Ballester Rodes, et al.	05-06-1997	
	A50	5,629,001		Michael, et al.	05-13-1997	
	A51	6,025,154		Li, et al.	02-15-2000	
	A52	6,353,004	Bl	Farrar, et al.	03-05-2002	
/	A53	6,469,030	B2	Farrer, et al.	10-22-2002	
7	A54	2001/0036951	Al	Farrar, et al.	11-01-2001	

FOREIGN PATENT DOCUMENTS

Examiner's Cite Initials No.	C:na	Foreign Patent Document			Name of Patentee or Applicant of Cited	Date of Publication of	Translation
		Office/ Country	Number	Kind Code	Document (not necessary)	Cited Document MM-DD-YYYY	(Y/N)
95	B22	AU	758,416		Arch Development Corp.	07-03-1999	
	B23	CA	2,312,234		Arch Development Corp.	05-14-1999	
	B24	DE	3,780,819	ļ			
1/9	B25	EP	1,047,726	A1	Quest International B.V.	07-22-1999	
175	B26	wo	99/22737	A1	Arch Development Corp.	05-14-1999	
105	B27	wo	04/043964	A2	Mallinckrodt	05-27-2004	

814319.1

Sheet

of

Phyllis Spirack 5/27/07

EODM DTC)-1449/A and B (M	lodified	APPLICATION NO.:	10/821,809	ATTY. DOCKET N	IO.: P0453.70116US01
	RMATION I		FILING DATE:	April 8, 2004	CONFIRMATION	NO.: 9063
	EMENT BY		APPLICANT:	Sanghvi et al.		
Sheet		of	 GROUP ART UNIT:	1614	EXAMINER:	Not Yet Assigned

OTHER ART - NON PATENT LITERATURE DOCUMENTS

(Yn) Cook, magazine, journal, serial, symposium, catalog, etc), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published. ALTIER et al., Opicid receptors in the ventral tegmental area contribute to stress-induced analgesia in the formalin tests for tonic pain. Brain Res. 1995 Apr 29/718(12):203-6. BAKER et al., Functional effects of systemically administered agonists and antagonists of mu, delta, and kappa opicid (receptor subhyses on body temperature in mice. 1 Pharmacol Exp Ther. 2002 Sep;302(3):1233-64. BOILE BASILISCO et al., Effect of Toperamide and naloxone on mouth-to-caecum transit time evaluated by lactulose hydrogen breath test. Gut. 1985 Jul;26(7):700-3. BOILE et al., Antiercone and nalitexone in thesis monkeys. 1 Pharmacol Exp Ther. 2002 Jul;302(1):247-73. BOWEN et al., College on Problems of Drug Dependence of eth Annual Scientific Meeting June 8-13, 2002. Quebec City, Quebec, Canada. Abstracts. Drug Alcohol Depend. 2002 May 1;66 Suppl 1:81-220. Abstract No. 55. C123 CARR et al., Nalitexone antagonizes the analgesic and immunosuppressive effects of morphine in mice. J Pharmacol Exp Ther. 1994 May;269(2):693-8. C124 CHOI et al., Opicid antagonizes review of their role in pallitative care, focusing on use in opicid-related constiguion. P Pain Symptom Manage. 2002 Jul;24(1):71-90. Review. C125 CHOI et al., Inhibition of chemokine-induced chemotaxis of monkey leukocytes by mu-opicid receptor gone in vivo. 1999 Sep-Oet;13(3):389-96. C126 DE PONTI et al., Methylnalitexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. Invited and proposition of hymnophyle trafficking. P Pharmacol Exp Ther. 1994 May;27(2):124-651. C127 FLORES et al., Guetemary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1993 Feb;10(1):11-13. C138 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 McAcK, Paralytic ileus: response to nalimanistration on Substances of A		I	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item	
Description of the publisher of the publ	Examiner's	Cite		Translation
C117 ALTIER et al., Oploid receptors in the ventral tegmental area contribute to stress-induced analgesia in the formalin test for tonic pain. Brain Res. 1996 Apr 297:181(2-)203-6. C118 BAKER et al., Functional effects of systemically administered agonists and antagonists of mu, delta, and kappa oploid receptor subtypes on body temperature in mite. J Pharmacel Exp Ther. 2002 Sep;302(3):1253-64. C129 BASILISCO et al., Grier of loperamide and naloxone on mouth-to-caecum transit time evaluated by lactulose hydrogen breath test. Gut. 1985 101;26(7):700-3. C120 BASILISCO et al., Effect of loperamide and naloxone on mouth-to-caecum transit time evaluated by lactulose hydrogen breath test. Gut. 1985 101;26(7):700-3. C121 BOWEN et al., Anlagonism of the antinociceptive and discriminative stimulus effects of heroin and morphine by 3-methoxynaltrexone and naltexone in rhesus monkeys. J Pharmacol Exp Ther. 2002 Jul;302(1):264-73. C122 BOWEN et al., College on Problems of Drup Dependence 64th Annual Scientific Meeting, June 8-13, 2002. Quebec City, Quebec, Canada. Abstracts. Drug Alcohol Depend. 2002 May 1;66 Suppl 1:S1-220. Abstract No. 65. C123 CARR et al., Naltrexone antagonizes the analgesis and immunosuppressive effects of morphine in mice. J Pharmacol Exp Ther. 1994 May;269(2):693-8. C124 CHOl et al., Opioid antagonists: a review of their role in palliative care, focusing on use in opioid-related constipation. J Pain Symptom Manage. 2002 Jul;24(1):71-90. Review. C125 CHOl et al., Inhibition of chemokine-induced immunosuppression: effect of acute morphine administration on lymphocyte trafficking. J Pharmacol Exp Ther. 1995 May;27(2):1246-51. C126 DE PONTI et al., Methylandtrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. C127 FLORES et al., Mechanisms of morphine-induced immunosuppression: effect of acute morphine administration on lymphocyte trafficking. J Pharmacol Exp Ther. 1995 May;27(2):1246-51. C128 GILES et al., Canadamina of morphine-induced immunosuppression: effect of acut			publisher, city and/or country where published.	(Y/N)
Color Formalin test for tonic pain. Brain Res. 1996 Apr 29/18(1-2):203-6.	0.	C117		
S	V> .			l l
opioid receptor subtypes on body temperature in mice. J Pharmacol Exp Ther. 2002 Sep;302(3):1253-64. C119 BASILISCO et al., Oral noloxone antagonizes loperamide-induced delay of orocceat transit. Dig Dis Sci. 1987 Aug;32(8):829-32. BASILISCO et al., Call 1983 Jul;26(7):700-3. BOWEN et al., Antagonism of the antinociceptive and discriminative stimulus effects of heroin and morphine by 3-methoxynaltrexone and naltrexone in rhesus monkeys. J Pharmacol Exp Ther. 2002 Jul;302(1):264-73. BOWEN et al., College on Problems of Drug Dependence 64th Annual Scientific Meeting. June 81, 2002. Quebec City, Quebec City	Oc	C118		
Dig Dis Sci. 1987 Aug;32(8):829-32. C120 BASLISCO et al., Effect of loperamide and naloxone on mouth-to-caecum transit time evaluated by lactulose hydrogen breath test. Gut. 1985 Jul;26(7):700-3. BOWEN et al., Antagonism of the antinociceptive and discriminative stimulus effects of heroin and morphine by 3-methoxynaltrexone and nalutrexone in flesus monkeys. J Pharmacol Exp Ther. 2002 Jul;302(1):264-73. C122 BOWEN et al., College on Problems of Drug Dependence 64th Annual Scientific Meeting. June 8-13, 2002. Quebec (City, Quebec, Canada. Abstracts. Drug Alcohol Depend. 2002 May 1;66 Suppl 1:S1-220. Abstract No. 63. C123 CARR et al., Naltrexone antagonizes the analgesic and immunosuppressive effects of morphine in micc. J Pharmacol Exp Ther. 1994 May;269(2):693-8. C124 CHOI et al., Opioid antagonists: a review of their role in pallitative care, focusing on use in opioid-related constipation. J Pain Symptom Manage. 2002 Jul;24(1):71-90. Review. C125 CHOI et al., Inhibition of chemokine-induced chemotaxis of monkey leukocytes by mu-opioid receptor agonists. In Vivo. 1999 Sep-Oct; 13(3):38-9-6. C126 DE PONTI et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. FLORES et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. FLORES et al., Methylnaltrexone Progenics Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. FLORES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;93(3-4):247-52. C126 GLES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;93(3-4):247-52. C137 KEHET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):38-10S. Review. C138 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of chanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse	']/>			
Dig Dis Sci. 1987 Aug;32(8):829-32. C120 BASILSCO et al., Effect of loperamide and naloxone on mouth-to-eaecum transit time evaluated by lactulose hydrogen breath test. Gut. 1985 Jul;26(7):700-3. G121 BOWEN et al., Antagonism of the antinociceptive and discriminative stimulus effects of heroin and morphine by 3-methoxynaltrexone and nalutexone in flesus monkeys. J Pharmacol Exp Ther. 2002 Jul;302(1):264-73. G122 BOWEN et al., College on Problems of Drug Dependence 64th Annual Scientific Meeting. June 8-13, 2002. Quebec (City, Quebec, Canada. Abstracts. Drug Alcohol Depend. 2002 May 1;66 Suppl 1:S1-220. Abstract No. 65. G123 CARR et al., Naltrexone antagonizes the analgesic and immunosuppressive effects of morphine in mice. J Pharmacol Exp Ther. 1994 May;269(2):693-8. C124 CH01 et al., Opioid antagonists: a review of their role in palliative care, focusing on use in opioid-related constipation. J Pain Symptom Manage. 2002 Jul;24(1):71-90. Review. C125 CH01 et al., Inhibition of chemokine-induced chemotaxis of monkey leukocytes by mu-opioid receptor agonists. In Vivo. 1999 Sep-Oct;13(3):38-9-6. C126 DE PONTI et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. C127 FLORES et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. G128 GILES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov. 25;93(3-4):247-52. G129 H0 et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. G130 KEHET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):38-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of chanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 NAMET et al., Naltrexone and morphine alter the discrimination and plasma levels of chanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C133 NAMET et al., Detect of a naloxone. Br J Surg. 1989 Oct;76(10	h	C119	BASILISCO et al., Oral naloxone antagonizes loperamide-induced delay of orocecal transit.	
hydrogen breath test. Gut. 1985 Jul;26(7):700-3. C121 BOWEN et al., Antagonism of the antinociceptive and discriminative stimulus effects of heroin and morphine by 3-methoxynaltrexone and naltrexone in rhesus monkeys. J Pharmacol Exp Ther. 2002 Jul;302(1):264-73. C122 BOWEN et al., College on Problems of Drug Dependence 64th Annual Scientific Meeting. June B-13, 2002. Quebec City, Quebec Ci	<u> 15</u>		Dig Dis Sci. 1987 Aug;32(8):829-32.	
C121 BOWEN et al., Antagonism of the antinociceptive and discriminative stimulus effects of heroin and morphine by 3-methoxynaltrexone and naltrexone in rhesus monkeys. J Pharmacol Exp Ther. 2002 Jul;302(1):264-73. BOWEN et al., College on Problems of Drug Dependence 64th Annual Scientific Meeting. June 8-13, 2002. Quebec City, Quebec, Canada. Abstracts. Drug Alcohol Depend. 2002 May 1;66 Suppl 1:S1-220. Abstract No. 65. C123 CARR et al., Naltrexone antagonizes the analgesics and immunosuppressive effects of morphine in mice. J Pharmacol Exp Ther. 1994 May;269(2):693-8. C124 CHOI et al., Opioid antagonists: a review of their role in palliative care, focusing on use in opioid-related constipation. J Pain Symptom Manage. 2002 Jul;24(1):71-90. Review. C125 CHOI et al., Inhibition of chemokine-induced chemotaxis of monky leukocytes by mu-opioid receptor agonists. In Vivo. 1999 Sep-Oct;13(5):389-96. C126 DE PONTI et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. C127 FLORES et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. C128 GILES et al., Quaternary opiate antagonists lower blood pressure and inhibit feucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25:95(3-4):247-52. C129 HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):35-10S. Review. C131 KEHLET et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1998 Feb;10(1):1-13. C132 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C133 L1 et al., Methadone chanaces human immunodefficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic Ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et a	1.00	C120	BASILISCO et al., Effect of loperamide and naloxone on mouth-to-caecum transit time evaluated by lactulose	
by 3-methoxynaltrexone and naltrexone in rhesus monkeys. J Pharmacol Exp Ther. 2002 Jul;302(1):264-73. C122 BOWEN et al., College on Problems of Drug Dependence 64th Annual Scientific Meeting. June 8-13, 2002. Quebec City, Quebec, Canada. Abstracts. Drug Alcohol Depend. 2002 May;166 Suppl 1:51-220. Abstract No. 65. C123 CARR et al., Naltrexone antagonizes the analgesic and immunosuppressive effects of morphine in mice. J Pharmacol Exp Ther. 1994 May;269(2):693-8. C124 CHOI et al., Opioid antagonists: a review of their role in palliative care, focusing on use in opioid-related constipation. J Pain Symptom Manage. 2002 Jul;24(1):71-90. Review. C125 CHOI et al., Inhibition of chemokine-induced chemotaxis of monkey leukocytes by mu-opioid receptor agonists. In Vivo. 1999 Sep-Oct;13(5):389-96. C126 DE PONTI et al., Methylinaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. C127 FLORES et al., Mechanisms of morphine-induced immunosuppression: effect of acute morphine administration on lymphocyte trafficking. J Pharmacol Exp Ther. 1995 Mar;27(3):1246-51. C128 GILES et al., Quatemary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52. C129 HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C133 Let al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substanc	'12>			
C122 BOWEN et al., College on Problems of Drug Dependence 64th Annual Scientific Meeting, June 8-13, 2002. Quebec City, Quebec, Canada. Abstracts. Drug Alcohol Depend. 2002 May 1;66 Suppl 1:S1-220. Abstract No. 65. CARR et al., Naltrexone antagonizes the analgesic and immunosuppressive effects of morphine in mice. J Pharmacol Exp Ther. 1994 May;269(2):693-8. C124 CHOI et al., Opioid antagonists: a review of their role in palliative care, focusing on use in opioid-related constipation. J Pain Symptom Manage. 2002 Jul;24(1):71-90. Review. C125 CHOI et al., Inhibition of chemokine-induced chemotaxis of monkey leukocytes by mu-opioid receptor agonists. In Vivo. 1999 Sep-Oct;13(5):389-96. C126 DE PONTI et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. FLORES et al., Mechanisms of morphine-induced immunosuppression: effect of acute morphine administration on hymphocyte trafficking. J Pharmacol Exp Ther. 1995 Mar;27(3):1246-51. C128 GILES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52. C129 Ho et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):38-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 LI et al., Methadone enhances human immunodefficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. DC C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AlDS, National Institute of Drug Research 96: Monograph Series. U.S. Depar	Ma	C121		1
Quebec City, Quebec, Canada. Abstracts. Drug Alcohol Depend. 2002 May 1;66 Suppl 1:S1-220. Abstract No. 65. C123 CARR et al., Naltrexone antagonizes the analgesic and immunosuppressive effects of morphine in mice. J Pharmacol Exp Ther. 1994 May;269(2):693-8. C124 CHO1 et al., Opioid antagonists: a review of their role in pallitative care, focusing on use in opioid-related constipation. J Pain Symptom Manage. 2002 Jul;24(1):71-90. Review. C125 CHO1 et al., Inhibition of chemokine-induced chemotaxis of monkey leukocytes by mu-opioid receptor agonists. In Vivo. 1999 Sep-Oct;13(5):389-96. C126 DE PONTI et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. FLORES et al., Mechanisms of morphine-induced immunosuppression: effect of acute morphine administration on lymphocyte trafficking. J Pharmacol Exp Ther. 1995 Mar;272(3):1246-51. C128 GILES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-41):247-52. C129 HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C131 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C131 Let al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan. 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic lieus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AlDS;	1/21		by 3-methoxynaltrexone and naltrexone in rhesus monkeys. J Pharmacol Exp Ther. 2002 Jul;302(1):264-73.	
65. C123 CARR et al., Naltrexone antagonizes the analgesic and immunosuppressive effects of morphine in mice. J Pharmacol Exp Ther. 1994 May;269(2):693-8. C124 CHOI et al., Opioid antagonists: a review of their role in palliative care, focusing on use in opioid-related constipation. J Pain Symptom Manage. 2002 Jul;24(1):71-90. Review. C125 CHOI et al., Inhibition of chemokine-induced chemotaxis of monkey leukocytes by mu-opioid receptor agonists. In Vivo. 1999 Sep-Oct;13(5):389-96. C126 DE PONTI et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. FLORES et al., Mechanisms of morphine-induced immunosuppression: effect of acute morphine administration on lymphocyte trafficking. J Pharmacol Exp Ther. 1993 Mar;272(3):1246-51. C128 GILES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52. FLORES et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. FLORES et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 MACK, Paralytic Ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C134 MACK, Paralytic Ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;4(4):415. C135 SANDNER-KEISLING et al., Pharmacology o	16	C122	BOWEN et al., College on Problems of Drug Dependence 64th Annual Scientific Meeting. June 8-13, 2002.	i
C123 CARR et al., Naltrexone antagonizes the analgesic and immunosuppressive effects of morphine in mice. J Pharmacol Exp Ther. 1994 May;269(2):693-8. C124 CHO et al., Opidio antagonists: a review of their role in palliative care, focusing on use in opioid-related constipation. J Pain Symptom Manage. 2002 Jul;24(1):71-90. Review. C125 CHO et al., Inhibition of chemokin-induced chemotaxis of monkey leukocytes by mu-opioid receptor agonists. In Vivo. 1999 Sep-Oct;13(5):389-96. C126 DE PONTT et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. C127 FLORES et al., Mechanisms of morphine-induced immunosuppression: effect of acute morphine administration on lymphocyte trafficking. J Pharmacol Exp Ther. 1995 Mar;272(2):1246-51. C128 GILES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52. C129 HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. C130 KEHLET et al., Review of postoperative iteus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 KAPIRAN et al., Number and morphine alter the discrimination of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic iteus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substrances of Abuse (1980) 1(2): 177-83. C136 PAHM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur P Pain. 2001;5(4):41	' 1E			i
Pharmacol Exp Ther. 1994 May;269(2):693-8. C124 CHOI et al., Opioid antagonists: a review of their role in palliative care, focusing on use in opioid-related constipation. J Pain Symptom Manage. 2002 Jul;24(1):71-90. Review. C125 CHOI et al., Inhibition of chemokine-induced chemotaxis of monkey leukocytes by mu-opioid receptor agonists. In Vivo. 1999 Sep-Oct;13(3):389-96. C126 DE PONTI et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. C127 FLORES et al., Mechanisms of morphine-induced immunosuppression: effect of acute morphine administration on lymphocyte trafficking. J Pharmacol Exp Ther. 1995 Mar;272(3):1246-51. C128 GILES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52. C129 HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 LI et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan.;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CDH+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical		ļ		
C124 CHOI et al., Opioid aniagonists: a review of their role in palliative care, focusing on use in opioid-related constipation. J Pain Symptom Manage. 2002 Jul;24(1):71-90. Review. C125 CHOI et al., Inhibition of chemokine-induced chemotaxis of monkey leukocytes by mu-opioid receptor agonists. In Vivo. 1999 Sep-Oct;13(5):389-96. C126 DE PONTI et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. C127 FLORES et al., Mechanisms of morphine-induced immunosuppression: effect of acute morphine administration on lymphocyte trafficking. J Pharmacol Exp Ther. 1995 Mar;27(2):1246-51. C128 GLES et al., Quaternary opinize antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52. C129 HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 L1 et al., Methadone enhances human immunodefficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;3(4):415-20. SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexo	100	C123		1
constipation. J Pain Symptom Manage. 2002 Jul;24(1):71-90. Review. C125 CHOI et al., Inhibition of chemokine-induced chemotaxis of monkey leukocytes by mu-opioid receptor agonists. In Vivo. 1999 Sep-Oct;13(5):389-96. C126 DE PONTI et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. FLORES et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. FLORES et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. FLORES et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. FLORES et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. FLORES et al., Quaternary opinte antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52. C129 HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:399-602. C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 Ll et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. SAKURADA et al., Differential antagonism				
C125 CHOI et al., Inhibition of chemokine-induced chemotaxis of monkey leukocytes by mu-opioid receptor agonists. In Vivo. 1999 Sep-Oct;13(5):389-96. C126 DE PONTI et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. C127 FLORES et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. C128 GILES et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. C128 GILES et al., Methanisms of morphine-induced immunosuppression: effect of acute morphine administration on lymphocyte trafficking. J Pharmacol Exp Ther. 1995 Mar;272(3):1246-51. C128 GILES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52. C129 HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 L1 et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;9	10	C124		1 1
agonists. In Vivo. 1999 Sep-Oct;13(5):389-96. C126 DE PONT1 et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. C127 FLORES et al., Mechanisms of morphine-induced immunosuppression: effect of acute morphine administration on lymphocyte trafficking. J Pharmacol Exp Ther. 1995 Mar;272(3):1246-51. C128 GLIES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52. C129 HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:399-602. C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 LI et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AlDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C139 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et a	19	ļ <u>.</u>		\vdash
In Vivo. 1999 Sep-Oct; 13(5):389-96. C126 DE PONTI et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. C127 FLORES et al., Mechanisms of morphine-induced immunosuppression: effect of acute morphine administration on lymphocyte trafficking. J Pharmacol Exp Ther. 1995 Mar;272(3):1246-51. C128 GILES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52. C129 HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 L1 et al., Methadone enhances human immunodefficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96; Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;3(4):415-20. C138 SANURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer ce	1′^	C125		1
C126 DE PONTI et al., Methylnaltrexone Progenics. Curr Opin Investig Drugs. 2002 Apr;3(4):614-20. Review. C127 FLORES et al., Mechanisms of morphine-induced immunosuppression: effect of acute morphine administration on lymphocyte trafficking. J Pharmacol Exp Ther. 1995 Mar;272(3):1246-51. C128 GILES et al., Quatermary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52. C129 HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 LI et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):956-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun	112			1 1
C127 FLORES et al., Mechanisms of morphine-induced immunosuppression: effect of acute morphine administration on lymphocyte trafficking. J Pharmacol Exp Ther. 1995 Mar;272(3):1246-51. C128 GILES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52. C129 HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 L1 et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C140 SHAVIT et al., Central and peripheral involvement of mu receptors in gastric secretory	~ /> -	0106		
on lymphocyte trafficking. J Pharmacol Exp Ther. 1995 Mar;272(3):1246-51. C128 GILES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52. C129 HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 LI et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylinaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Doc;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	<u> </u>			
C128 GILES et al., Quaternary opiate antagonists lower blood pressure and inhibit leucine-enkephalin responses. Eur J Pharmacol. 1983 Nov 25;95(3-4):247-52. C129 HO et al., Suppression of immunological functions in morphine addicted mice. NIDA Res Monogr. 1986;75:599-602. C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 LI et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	1 hc	C127		1 1
J Pharmacol. 1983 Nov 25;95(3-4):247-52.	1 1/2			
1986;75:599-602. C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTEC, CAS Abstract Document No. 127: 13345, 1997. C133 LI et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	1/25	C128		
C130 KEHLET et al., Review of postoperative ileus. Am J Surg. 2001 Nov;182(5A Suppl):3S-10S. Review. C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 LI et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	PcT	C129		
C131 KOSTEN et al., Naltrexone and morphine alter the discrimination and plasma levels of ethanol. Behav Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 LI et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	100	C130		
Pharmacol. 1999 Feb;10(1):1-13. C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 L1 et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	_\/> -			
C132 KOSTIC, CAS Abstract Document No. 127: 13345, 1997. C133 LI et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	121	C131		1
C133 LI et al., Methadone enhances human immunodeficiency virus infection of human immune cells. J Infect Dis. 2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec; 1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	170	C122		
2002 Jan 1;185(1):118-22. Epub 2001 Dec 14. C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	1 12			
C134 MACK, Paralytic ileus: response to naloxone. Br J Surg. 1989 Oct;76(10):1101. C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	1/51	L133	1 '	1
C135 NEMETH-LEFKOWITZ et al., Research communication in Substances of Abuse (1980) 1(2): 177-83. C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.		C124		
C136 PHAM et al., Drugs of Abuse: Chemistry, Pharmacology, Immunology and AIDS; National Institute of Drug Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	- 1 1/2 -			
Research 96: Monograph Series. U.S. Department of Health and Human Services; 1990. C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	μ 2			\vdash
C137 QUANG-CONTAGREL et al., Long-term methadone treatment: effect on CD4+ lymphocyte counts and HIV-1 plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	1 50	U136		
plasma RNA level in patients with HIV infection. Eur J Pain. 2001;5(4):415-20. C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	. 4) >	C127		
C138 SAKURADA et al., Differential antagonism of endomorphin-1 and endomorphin-2 supraspinal antinociception by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	100	(13/		
by naloxonazine and 3-methylnaltrexone. Peptides. 2002 May;23(5):895-901. C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	- \9-2 -	C120		
C139 SANDNER-KEISLING et al., Pharmacology of opioid inhibition to noxious uterine cervical distension. Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	b<	C138		
Anesthesiology. 2002 Oct;97(4):966-71. C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.		C130		
C140 SHAVIT et al., Effects of a single administration of morphine or footshock stress on natural killer cell cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	19	(137		1 1
cytotoxicity. Brain Behav Immun. 1987 Dec;1(4):318-28. C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.		C140		
C141 SOLDANI et al., Central and peripheral involvement of mu receptors in gastric secretory effects of opioids in the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.	IWS	1 0140		
the dog. Eur J Pharmacol. 1985 Nov 19;117(3):295-301.		C141		
	TVS	1 2,3,		
	<u> </u>	C142	STEINBROOK et al., An opioid antagonist for postoperative ileus. N Engl J Med. 2001 Sep 27;345(13):988-9.	

814319.1

P.Spirack 5/27/07

FORM PTO-1449/A and B (Modified)

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

Sheet 3 of 3

APPLICATION NO.: 10/821,809 ATTY. DOCKET NO.: P0453.70116US01

FILING DATE: April 8, 2004 CONFIRMATION NO.: 9063

APPLICANT: Sanghvi et al.

GROUP ART UNIT: 1614 EXAMINER: Not Yet Assigned

()5	C143	WEI et al., Abstracts of the 2002 Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics. Atlanta, Georgia, USA. March 24-27, 2002. Clin Pharmacol Ther. 2002 Feb;71(2):P1-136.	
125	C144	WILMORE et al., Can we minimize the effects of opioids on the bowel and still achieve adequate pain control? Am J Surg. 2001 Nov;182(5A Suppl):1S-2S.	
1 PS	C145	WYBRAN et al., Suggestive evidence for receptors for morphine and methionine-enkephalin on normal human blood T lymphocytes. J Immunol. 1979 Sep;123(3):1068-70.	
D51	C146	YUAN, Clinical Status of Methylnaltrexone, A New Agent to Prevent and Manage Opioid-Induced Side Effects. J Support Oncol. 2004 Mar/Apr: 2(2):111-22.	

EXAMINE R DATE CONSIDERED (2)
TEXAMILIER MILL TILL A // A IL I / L'DATE CONSIDERED A
PANITO K STORY OF THE CONSIDERED STOTION
1. IVILAY VIX X VIXIVIL CK 572+10+

#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

[NOTE - The Office hereby waives the requirement under 37 CFR 1.98 (a)(2)(i) for submitting a copy of each cited U.S. patent and each U.S. patent application publication for all U.S. national patent applications filed after June 30, 2003 and for all international applications that have entered the national stage under 35 USC 371 after June 30, 2003. See 37 CFR 1.491(b). For all patent applications filed on or before June 30, 2003, copies of cited U.S. patents and patent application publications are still required unless an eIDS is filed. Copies of all other patent(s), publication(s), or other information listed must still be provided, even if it was previously submitted to, or cited by, the U.S. Patent Office in an earlier application, unless the earlier application is identified by the IDS and is relied upon for an earlier filing date under 35 U.S.C. §120, and the copy was provided in the earlier application.]

[•]a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. ___, filed ___, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

		<u>/c</u>				
EODM DTO)-1449/A and B (M	/	13 2004	APPLICATION NO.:	10/821,809	ATTY. DOCKET NO.: P0453.70116US01
INFO		TCC!		FILING DATE:	April 8, 2004	CONFIRMATION NO.: 9063
STAT	RMATION D EMENT BY	APP	LICANT	APPLICANT:	Sanghvi et al.	
				GROUP ART UNIT:	1614	EXAMINER: CDIVACK
Sheet	1	of	1			SYIVACK

U.S. PATENT DOCUMENTS

Examiner's	Cite	U.S. Patent Document		Name of Patentee or Applicant of Cited	Date of Publication or of issue	
Initials	No.	Number	Kind Code	Document	of Cited Document MM-DD-YYYY	
75	A55	5,804,595		Portoghese, et al.	09-08-1998	
105	A56	5,866,154	ļ.	Bahal, et al.	02-02-1999	
105	A57	2003-0022909	A1	Moss, et al.	01-30-2003	
125	A58	2003-0124086	Al	Bentley, et al.	07-03-2003	
1)0	A59	2003-0191147	Al	Sherman, et al.	10-09-2003	

FOREIGN PATENT DOCUMENTS

Examiner's Cite Initials No.		Foreign Patent Document			Name of Patentee or Applicant of Cited	Date of Publication of	Translation
		Office/ Number Kind Code			Document (not necessary)	Cited Document MM-DD-YYYY	(Y/N)
1/5	B28	CA	2,064,373		Lilly (Eli) and Company	09-30-1992	
1)C	B29	EP	506,468	A1	Eli Lilly and Company	09-30-1992	
100	B30	EP	643,967	A2	Euro Celtique S.A.	03-22-1995	
75	B31	wo	01/32180	A2	Rodeva Limited	05-10-2001	
051	B32	wo	02/098422	A1	University of Chicago	12-12-2002	
196	B33	wo	03/032990	A2	Shearwater Corporation	04-24-2003	
25.	B34	wo	2004/014291	A2	Moss	02-19-2004	

OTHER ART - NON PATENT LITERATURE DOCUMENTS

Examiner's Initials	Cite No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Transla (Y/I	
PS	C147	FARTHING et al., New drugs in the management of the irritable bowel syndrome. Drugs. 1998 Jul;56(1):11-21. Review.		
105	C148	FINGL et al., Chapter 43: Laxatives and cathartics. In Pharmacological Basis of Therapeutics. 1980: 1002-5.		
13	C149	SCHUBERT-ZSILAVECZ et al., Das reizdarmsyndrom irritable bowel syndrome. Deutsche apotheker zeitung. 2002 Aug 22; 142(34): 40-9.	Ye	s
13	C150	TALLEY et al., Pharmacologic therapy for the irritable bowel syndrome. Am J Gastroenterol. 2003 Apr;98(4):750-8. Review.		
105	C151	THOMPSON et al., Laxatives: clinical pharmacology and rational use. Drugs. 1980 Jan;19(1):49-58. Review.		

EXAMINER:	DATE CONSIDERED:	127/m
PMIIS >MACK	5	LT10+

#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

[NOTE - The Office hereby waives the requirement under 37 CFR 1.98 (a)(2)(i) for submitting a copy of each cited U.S. patent and each U.S. patent application publication for all U.S. national patent applications filed after June 30, 2003 and for all international applications that have entered the national stage under 35 USC 371 after June 30, 2003. See 37 CFR 1.491(b). For all patent applications filed on or before June 30, 2003, copies of cited U.S. patents and patent application publications are still required unless an eIDS is filed. Copies of all other patent(s), publication(s), or other information listed must still be provided, even if it was previously submitted to, or cited by, the U.S. Patent Office in an earlier application, unless the earlier application is identified by the IDS and is relied upon for an earlier filing date under 35 U.S.C. §120, and the copy was provided in the earlier application.]

[•]a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. ___, filed ___, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation-in-part, and divisional applications).

APPLICATION NO.: 10/821,809 ATTY. DOCKET NO.: P0453.70116US01 FORM PTO-1449/A and B (modified PTO/SB/08) **FILING DATE:** April 8, 2004 INFORMATION DISCLOSURE

CONFIRMATION NO.: 9063

APPLICANT: Sanghvi et al.

GROUP ART UNIT: 1614 **EXAMINER:** Phyllis G. Spivack of

FEB 2.3 2007

Sheet

STATEMENT BY APPLICANT

City		T		PATENT DOCUMENTS		
Initials	Cite No.	U.S. Patent Docume	Kind Code	Name of Patentee or Applicant of Cited Document	Date of Publication or Issue of Cited Document MM-DD-YYYY	
1/5		4,322,426		Hermann et al.	03-30-1982	
1		4,965,269		Brändström et al.	10-23-1990	
		5,159,081		Cantrell et al.	10-27-1992	
		5,202,159		Chen et al.	04-13-1993	
		5,391,372		Campbell	02-21-1995	
		5,614,219	*3.	Wunderlich et al.	03-25-1997	
		5,656,290	·	Kelm et al.	08-12-1997	
		5,981,185		Matson et al.	11-09-1999	
	·	6,455,537		Cooper	09-24-2002	
		6,986,901		Meisel et al.	01-17-2006	
		2002-0064771	Al	Zhong et al.	05-30-2002	
		2003-0026801	Al	Weiner et al.	02-06-2003	
		2003-0065003	Al	Foss et al.	04-03-2003	
		2003-0187010	A1	Foss et al.	10-02-2003	
		2004-0162306	A1	Foss et al.	08-19-2004	
		2004-0162307	A1	Foss et al.	08-19-2004	
		2004-0162308	A1	Foss et al.	08-19-2004	
		2004-0167147	A1	Foss et al.	08-26-2004	
		2004-0167148	Al	Foss et al.	08-26-2004	
		2004-0259899	Al	Sanghvi et al.	12-23-2004	
		2004-0266806	Al	Sanghvi et al.	12-30-2004	
		2005-0004155	Al	Boyd et al.	01-06-2005	
		2005-0048117	Al	Foss et al.	03-03-2005	
		2005-0124885	Al	Abend et al.	06-09-2005	
		2006-0205753	Al	Israel	09-14-2006	
V						

FOREIGN PATENT DOCUMENTS

Examiner's	Cite	Foreign Patent Document			Name of Patentee or Applicant of Cited	Date of Publication of	Translation
Initials #	No.	Office/ Country	Number	Kind Code	Document	Cited Document MM-DD-YYYY	(Y/N)
		DE	196 51 551	Al	Klinge Pharm GmbH	06-18-1998	Y-Abstract
73		EP	0 289 070		Duphair International Research B.V.	11-02-1988	

EXAMINER:

DATE CONSIDERED:

^{*}EXAMINER: Initial if reference considered, whether or notitation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449/A and B (modified PTO/SB/08) INFORMATION DISCLOSURE					APPLICATION NO.:	10/821,809	ATTY. DOCKET N	O.: P0453.70116US01
					FILING DATE:	April 8, 2004	CONFIRMATION	NO.: 9063
STATEMENT BY APPLICANT					APPLICANT:	Sanghvi et al.		
Sheet 2 of 4			GROUP ART UNIT:	1614	EXAMINER:	Phyllis G. Spivack		
	·			· · · · · · · · · · · · · · · · · · ·			1	

VS	wo	96/14058	Αl	Euroceltique, S.A.	05-17-1996	
1 75	wo	2004/091623	A1	Progenics Pharmaceuticals, Inc.	10-28-2004	

OTHER ART — NON PATENT LITERATURE DOCUMENTS

Examiner's Initials #			Translation (Y/N)
De			
12		Remington's Pharmaceutical Sciences, 15 th Edition, 1925:1614-5.	
1 1/5 1		Progenics initiates second phase 3 clinical trial of methylnaltrexone in opioid- induced constipation. Press Release. Progenics Pharmaceuticals, Inc. January 13, 2004.	
1-1-		rogenics achieves enrollment target in pivotal phase 3 clinical trial of	
05		methylnaltrexone to opioid-induced constipation. Press Release. Progenics Pharmaceuticals, Inc. December 3, 2004.	
25		Progenics announces positive top-line results from pivotal phase 3 clinical trial or MNTX in opioid-induced constipation. Press Release. Progenics Pharmaceuticals, Inc. March 10, 2005.	
PS		AUNG et al., Methylnaltrexone prevents morphine-induced kaolin intake in the rat. Life Sci. 2004 Apr 16;74(22):2685-91.	
75		BROWN et al., Techniques for mechanical stimulation of cells in vitro: a review. J Biomech. 2000 Jan;33(1):3-14.	
105		EGAN et al., Prospective pharmacokinetic and pharmacodynamic validation of propofol's context sensitive T1/2. Anesthesiology. 1999 Sep;91(3A): Abstract A347.	
B		FOSS et al., The efficacy or oral methylnaltrexone in decreasing the subjective effects of IV morphine. Anesth Analg. 1997;84. Abstract S484.	
PS		FOSS et al., Enteric-coated methylnaltrexone prevents opioid-induced oral-cecal transit delay in humans. Anesth Analg. 2000;90. Abstract S409.	
18		FOSS et al., Subcutaneous methylnaltrexone reduces morphine-induced subjective effects in humans. Anesthesiology. 2001;95. Abstract A-817.	
125		FRANCE et al., Morphine, saline and naltrexone discrimination in morphine-treated pigeons. J Pharm and Exper Ther. 1987;242:195-202.	
DS		FUNKE et al., A proton and carbon-13 nuclear magnetic resonance study of three quaternary salts of naloxone and oxymorphone. J Chem Soc. 1986:735-8.	
Ps		GUTSTEIN et al., Role of inositol 1,4,5-trisphosphate receptors in regulating apoptotic signaling and heart failure. Heart Vessels. 1997;Suppl 12:53-7.	
P5		HICKS et al., Differential effects of the novel non-peptidic opioid 4-tyrosylamido-6-benzyl-1,2,3,4 tetrahydroquinoline (CGPM-9) on in vitro rat t lymphocyte and macrophage functions. Life Sci. 2001 May 4;68(24):2685-94.	
PS		HIROTA et al., Loss of a gp130 cardiac muscle cell survival pathway is a critical event in the onset of heart failure during biomechanical stress. Cell. 1999 Apr 16;97(2):189-98.	
09		HO et al., Beta-endorphin: peripheral opioid activity of homologues from six species. Int J Pept Protein Res. 1987 Apr;29(4):521-4.	

EXAMINER: Ph	ullis Sawack	DATE CONSIDERED:	7/07
			· · · · · · · · · · · · · · · · · · ·

[&]quot;EXAMINER: Initial if reference considered, whether or notitation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449/A and B (modified PTO/SB/08)				APPLICATION NO.:	10/821,809	ATTY. DOCKET NO	D.: P0453.70116US01
INFORMATION DISCLOSURE STATEMENT BY APPLICANT			FILING DATE:	April 8, 2004	CONFIRMATION	O.: 9063	
			APPLICANT:	Sanghvi et al.			
Sheet	3	of	4	GROUP ART UNIT:	1614	EXAMINER:	Phyllis G. Spivack

	HO et al., Methylnaltrexone antagonizes opioid-mediated enhancement of HIV infection of human	
P5	blood mononuclear phagocytes. J Pharmacol Exp Ther. 2003 Dec;307(3):1158-62.	
	HOFMANN et al., Hypocalcemia during restraint stress in rats. Indication that gastric ulcer	
P5	prophylaxis by exogenous calcium interferes with calcitonin release. Res Exp Med (Berl). 1979	
	May 30;175(2):159-68.	
D-	HUSSAIN et al., Improvement of the oral bioavailability of naltrexone in dogs: a prodrug approach.	
Ps	J Pharm Sci. 1987 May;76(5):356-8.	
l L I	HUSSAIN et al., Naltrexone-3-salicylate (a prodrug of naltrexone): synthesis and pharmacokinetics	
P5	in dogs. Pharm Res. 1988 Feb;5(2):113-5.	
	IORIO et al., Narcotic agonist/antagonist properties of quaternary diastereoisomers derived from	
1 PS	oxymorphone and naloxone. Eur J Med Chem. 1984;19(4):301-3.	
,	LOPEZ et al., Demonstration of long-lasting blockade of experimental ileus in rats by an opioid k-	
PS	agonist. Gastroenterology. 1995;108(4):A640. Abstract.	
7	MCCARTHY et al., Preliminary studies on the use of plasma β-endorphin in horses as an indicator	
1 Ds	of stress and pain. J Equine Vet Sci. 1993;13(4):216-9.	
100	MIEDEMA et al., Methods for decreasing postoperative gut dysmotility. Lancet Oncol. 2003	
PS	Jun;4(6):365-72.	
	MOSS et al., Methylnaltrexone prevents morphine-induced CCR5 receptor expression.	
18	Anesthesiology. 2003;99. Abstract A-961.	
De	PAPAPETROPOULOS et al., Nitric oxide synthase inhibitors attenuate transforming-growth-	
PS	factor-beta 1-stimulated capillary organization in vitro. Am J Pathol. 1997 May;150(5):1835-44.	
7 7	RESNICK et al., Delayed gastric emptying and postoperative ileus after nongastric abdominal	
195	surgery: part I. Am J Gastroenterol. 1997 May;92(5):751-62.	
	RESNICK et al., Delayed gastric emptying and postoperative ileus after nongastric abdominal	
Ps	surgery: part II. Am J Gastroenterol. 1997 Jun;92(6):934-40.	L
00	STEPHENSON et al., Methylnaltrexone reverses opioid-induced constipation. Lancet Oncol. 2002	
1/2	Apr;3(4):202.	
100	THOMAS et al., Amelioration of peripheral side effects of opioids: clinical experience with	
1/5	methylnaltrexone (MNTX). Proc World Congr Anesth. 2004:107.	<u> </u>
Oc	TOMIYASU et al., Analysis of intercostal nerve damage associated with chronic post-thoracotomy	1
125	pain. Anesthesiology. 2001;95. Abstract A-964.	
	WEI et al., Opioid-induced immunosuppression: is it centrally mediated or peripherally mediated?	1
195	Biochem Pharmacol. 2003 Jun 1;65(11):1761-6.	
	WEI et al., Pharmacokinetics of subcutaneous methylnaltrexone: different route administration	
100	comparison. 2001. ASA Annual Meeting Abstracts. October 14-18, 2001. Chicago, IL. Abstract A-	· ·
PS	962.	
00	YUAN et al., Gut and brain effects of American ginseng root on brainstem neuronal activities in	
19	rats. Amer J Chin Med. 1998; 26: 47-55.	
7	YUAN et al., Methylnaltrexone (MNTX) for chronic opioid-induced constipation. 2002 ASCO	
PS	Annual Meeting. Proc Am Soc Clin Oncol. 2002;21:376a. Abstract 1501.	
カー	YUAN et al., Safety and tolerance of oral methylnaltrexone in healthy volunteers. Anesth Analg.	
1/5	1997;84:S1-599. Abstract S574.	1
		l

EXAMINER: Phulis Savack	DATE CONSIDERED: 5/27/07

[&]quot;EXAMINER: Initial if reference considered, whether or noticitation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO)_1449/A and B (m	nodified	PTO/SB/08)	APPLICATION NO.:	10/821,809	ATTY. DOCKET N	IO.: P0453.70116US01
FORM PTO-1449/A and B (modified PTO/SB/08) INFORMATION DISCLOSURE				FILING DATE:	April 8, 2004	CONFIRMATION	NO.: 9063
STATEMENT BY APPLICANT			APPLICANT:	Sanghvi et al.			
Sheet	4	of	4	GROUP ART UNIT:	1614	EXAMINER:	Phyllis G. Spivack

PS	YUAN et al., Methylnaltrexone changes gut motility and transit time in chronic methadone-maintained subjects. Anesth Analg. 1999;88: S1-424. Abstract S404.	
PS	YUAN et al., Antagonism of chronic opioid-induce gut effects. Anesth Analg. 2000;90:S1-523. Abstract S479.	
PS	YUAN et al., Pharmacokinetics of intravenous vs. oral methylnaltrexone: evidence for direct gut effects. Anesth Analg. 2001;92: S1-363. Abstract S274.	
PS	YUAN et al., Oral methylnaltrexone reverses morphine-induced changes in gastrointestinal motility. Anesthesiology. 1996 Sep;85(3A). Abstract A335.	
PS	YUAN et al., Oral methylnaltrexone reverses chronic opioid-induced constipation. Anesthesiology. 2000 Sep;93(3A). Abstract A-872.	
PS	YUAN et al., Subcutaneous methylnaltrexone prevents morphine-induced delay in gut transit time: a clinical trial. Anesthesiology. 2001;95. Abstract A-963.	
25	YUAN et al., Methylnaltrexone prevents morphine-induced kaolin intake in the rat. Anesthesiology. 2003;99. Abstract A-922.	
75	YUAN et al., Dose-related effects of oral acetaminophen on cold-induced pain: a double-blind, randomized, placebo-controlled trial. Clin Pharmacol Ther. 1998, Mar;63(3):379-83.	
951	YUAN et al., Gastric effects of mu-, delta- and kappa-opioid receptor agonists on brainstem unitary responses in the neonatal rat. Eur J Pharmacol. 1996 Oct 24;314(1-2):27-32.	
PS	YUAN et al., Effects of low-dose morphine on gastric emptying in healthy volunteers. J Clin Pharmacol. 1998 Nov;38(11):1017-20.	
25	YUAN et al., Gut motility and transit changes in patients receiving long-term methadone maintenance. J Clin Pharmacol. 1998 Oct;38(10):931-5.	
1/25	YUAN et al., Tolerability, gut effects, and pharmacokinetics of methylnaltrexone following repeated intravenous administration in humans. J Clin Pharmacol. 2005 May;45(5):538-46.	
13	YUAN et al., Antagonism of gastrointestinal opioid effects. Reg Anesth Pain Med. 2000 Nov-Dec;25(6):639-42.	
13	YUAN et al., Methylnaltrexone reduces oral-cecal transit time in humans. Dig Dis Week Abstr. 2003:A-578. Abstract T1840.	
13	YUAN et al., Opioid analgesia without gut side effects: effects of methylnaltrexone as a novel peripheral opioid antagonist. Assoc Univ Anesth Abst. 2003: PD2.	
25	YUAN et al., Pain control with side effects: clinical studies on methylnaltrexone as a novel peripheral opioid antagonist. 7 th America-Japan Anesth Congr. Yamanashi, Japan. 2002:41.	

^{*}a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. ___, filed ___, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation-in-part, and divisional applications).

[NOTE -- No copies of U.S. patents, published U.S. patent applications, or pending, unpublished patent applications stored in the USPTO's Image File Wrapper (IFW) system, are included. See 37 CFR §1.98 and 1287OG163. Copies of all other patent(s), publication(s), unpublished, pending U.S. patent applications, or other information listed are provided as required by 37 CFR §1.98 unless 1) such copies were provided in an IDS in an earlier application that complies with 37 CFR §1.98, and 2) the earlier application is relied upon for an earlier filing date under 35 U.S.C. §120.]

	EXAMINER: PM	11/1/is SWACK	DATE CONSIDERED:	
--	--------------	---------------	------------------	--

^{*}EXAMINER: Initial if reference considered, whether or noticitation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.